

# PATENT COOPERATION TREATY

# PCT

## INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

Applicant's or agent's file reference 28927.0019	<b>FOR FURTHER ACTION</b>	See item 4 below
International application No. PCT/US2005/010441	International filing date ( <i>day/month/year</i> ) 28 March 2005 (28.03.2005)	Priority date ( <i>day/month/year</i> ) 26 March 2004 (26.03.2004)
International Patent Classification (8th edition unless older edition indicated) See relevant information in Form PCT/ISA/237		
Applicant VAN ANDEL RESEARCH INSTITUTE		

1.	This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 <i>bis</i> .1(a).																								
2.	This REPORT consists of a total of 8 sheets, including this cover sheet.  In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.																								
3.	<p>This report contains indications relating to the following items:</p> <table style="width: 100%;"> <tr> <td style="width: 10%; text-align: center;"><input checked="" type="checkbox"/></td> <td style="width: 30%;">Box No. I</td> <td style="width: 60%;">Basis of the report</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. II</td> <td>Priority</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. III</td> <td>Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. IV</td> <td>Lack of unity of invention</td> </tr> <tr> <td style="text-align: center;"><input checked="" type="checkbox"/></td> <td>Box No. V</td> <td>Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VI</td> <td>Certain documents cited</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VII</td> <td>Certain defects in the international application</td> </tr> <tr> <td style="text-align: center;"><input type="checkbox"/></td> <td>Box No. VIII</td> <td>Certain observations on the international application</td> </tr> </table>	<input checked="" type="checkbox"/>	Box No. I	Basis of the report	<input type="checkbox"/>	Box No. II	Priority	<input checked="" type="checkbox"/>	Box No. III	Non-establishment of opinion with regard to novelty, inventive step and industrial applicability	<input type="checkbox"/>	Box No. IV	Lack of unity of invention	<input checked="" type="checkbox"/>	Box No. V	Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement	<input type="checkbox"/>	Box No. VI	Certain documents cited	<input type="checkbox"/>	Box No. VII	Certain defects in the international application	<input type="checkbox"/>	Box No. VIII	Certain observations on the international application
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<input type="checkbox"/>	Box No. VIII	Certain observations on the international application																							
4.	The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).																								

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date of issuance of this report 26 September 2006 (26.09.2006)
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e-mail: pt02@wipo.int	

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

REC'D 27 JAN 2006

WIPO

PCT

PCT

To:

see form PCT/ISA/220

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY (PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

**FOR FURTHER ACTION**  
See paragraph 2 below

International application No.  
PCT/US2005/010441

International filing date (day/month/year)  
28.03.2005

Priority date (day/month/year)  
26.03.2004

International Patent Classification (IPC) or both national classification and IPC  
C12N15/11, C12N15/86

Applicant  
VAN ANDEL RESEARCH INSTITUTE

### 1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

### 3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office  
D-80298 Munich  
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Surdej, P

Telephone No. +49 89 2399-7334



**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/010441

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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/US2005/010441

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**Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

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The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 1-3, 8-47 (all partially), 4-6 (all completely)

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the whole application or for said claims Nos. 1-3, 8-47 (all partially), 4-6 (all completely)
- ☒ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:
- |                            |   |
|----------------------------|---|
| the written form           | <input type="checkbox"/> has not been furnished                       |
|                            | <input checked="" type="checkbox"/> does not comply with the standard |
| the computer readable form | <input checked="" type="checkbox"/> has not been furnished            |
|                            | <input type="checkbox"/> does not comply with the standard            |
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.
- ☐ See separate sheet for further details

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

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PCT/US2005/010441.

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(I) with regard to novelty, inventive step or  
Industrial applicability; citations and explanations supporting such statement**

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1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-3, 8-11, 14-16, 21-47 (all partially)
Inventive step (IS)	Yes: Claims	
	No: Claims	1-3, 8-47 (all partially)
Industrial applicability (IA)	Yes: Claims	1-3, 8-47 (all partially)
	No: Claims	

2. Citations and explanations

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/010441

Reference is made to the following documents:

- D1: WO 2004/007754 A (RIGEL PHARMACEUTICALS, INC; HITOSHI, YASUMICHI; JENKINS, YONCHU; MARKO) 22 January 2004 (2004-01-22)
- D2: WO 2004/020583 A (BRISTOL-MYERS SQUIBB COMPANY; HUANG, FEI; HAN, XIA; REEVES, KAREN, A;) 11 March 2004 (2004-03-11)
- D3: ABOUNADER R ET AL: "In vivo targeting of SF/HGF and c-met expression via U1 snRNA/ribozymes inhibits glioma growth and angiogenesis and promotes apoptosis" FASEB JOURNAL (FEDERATION OF AMERICAN SOCIETIES FOR EXPERIMENTAL BIOLOGY), BETHESDA, US, vol. 16, no. 1, January 2002 (2002-01), pages 108-110, XP002249673 ISSN: 0892-6638
- D4: MA P C ET AL: "c-Met: Structure, functions and potential for therapeutic inhibition" CANCER AND METASTASIS REVIEWS, KLUWER ACADEMIC PUBLISHERS, DORDRECHT, NL, vol. 22, no. 4, December 2003 (2003-12), pages 309-325, XP002328700 ISSN: 0167-7659
- D5: SHINOMIYA NARIYOSHI ET AL: "RNA interference reveals that ligand-independent met activity is required for tumor cell signaling and survival" CANCER RESEARCH, vol. 64, no. 21, 1 November 2004 (2004-11-01), pages 7962-7970, XP002361319 ISSN: 0008-5472

**Introduction**

The application discloses an interfering RNA (RNAi) molecule having a sequence that is sufficiently complementary to the sequence of mRNA encoded by human c-met, murine c-met, or c-met of another mammalian source, so that expression of said RNAi molecule in a cell that normally expresses c-met results in diminution or loss of expression of said mRNA and uses thereof.

The application draws priority from one priority document which has the priority date 26 March 2004 (P1).

**Re Item II**

**Priority**

1. The application draws priority from an earlier application P1 and said priority appears

to be valid, D5 will be thus not consider for the claimed subject matter.

**Re Item III**

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2. No search report was established on the subject-matter of claims 1-3, 8-47 (all partially), 4-6 (all completely)(Rule 66.1(e) PCT) since the specific sequences of claims 1-7 have, according to PCT Rule 13ter.1.d, not been searched since the sequence listing as present in the description does not comply with WIPO Standard ST 25 prescribed in the administrative instructions under Rule 5.2. The sequence listing has been furnished neither in paper form nor in machine readable form as provided for in the same instructions and the applicant has not remedied the disclosed deficiencies within the limit fixed in the invitation pursuant to Rule 13ter.1.a. The search was therefore limited to RNAi having sequence complementary to mRNA encoded by human c-met, murine c-met, or c-met of another mammalian source, so that expression of said RNAi molecule in a cell that normally expresses c-met results in diminution or loss of expression of said mRNA. For the search, c-met was understood from the description as Met proto-oncogene tyrosine kinase, receptor of scatter factor/hepatocyte growth factor. Therefore, only the subject-matter of claims 1-3, 8-47 (all partially) as limited for the search is considered herein.
3. Claims 21-38 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

**Re Item V**

Reasoned statement Article 35(2) PCT with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

Novelty and inventive step (Art. 33(1)-(3) PCT)

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING  
AUTHORITY (SEPARATE SHEET)**

International application No.

PCT/US2005/010441

4. Claims 1-3, 8-11, 14-16, 21-47 (all partially) are not new in view of D1 and D2. An interfering RNA (RNAi) molecule having a sequence that is sufficiently complementary to the sequence of mRNA encoded by human c-met, murine c-met, or c-met of another mammalian source, so that expression of said RNAi molecule in a cell that normally expresses c-met results in diminution or loss of expression of said mRNA is disclosed in D1 and D2 (e.g. D1: paragraphs 3, 5, 22, 272, fig. 6, D2: page 10, lines 11-21, pages 97-98).
5. The subject-matter of claims 12-13, 17-20 is new but not inventive. The subject-matter of said claims appears to be trivial for the skilled person armed with the disclosures D1 and D2.

**Industrial Applicability (Art. 33. (1) and (4) PCT)**

6. For the assessment of the present claims 21-38 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.